

REMARKS

Upon entry of the foregoing amendment, claims 10–32 are pending for the Examiner’s consideration with claims 10, 25 and 26 being the independent claims. The Office Action withdraws claims 10-24. Claims 25-32 stand rejected. Claims 10, 25 and 26 are amended herein. Applicants respectfully submit that the present amendment introduces no new matter. In this regard, the Examiner is referred to the application as originally filed at, for example, Table A, pages 3-4; page 5, line 1 to page 6, line 15; and page 15, line 30 to page 16, line 32.

Applicants also submit a Substitute Specification along with the instant Amendment. It is believed that these changes to the specification do not involve the introduction of new matter. Accordingly, entry of these changes is respectfully requested.

Withdrawal of Claims 10-24

The Office Action withdraws claims 10-24 and states that “new claims 10-24 correspond to non-elected invention of Group III in the restriction requirement mailed January 19, 2006 Claims 25-32 are interpreted as directed to *in silico* methods of identifying drug candidates.” The Office Action identified Group III in the restriction requirement as original “[c]laims 3 and 4, drawn to a method of using the crystal to identify modulator of HPTPbeta activity”

Applicants respectfully disagree with the position that claims 10-24 correspond to non-elected Group III. Claims 10-24 clearly fall within the definition of elected Group II, which was identified in the restriction requirement as “a method of identifying modulator of HPTPbeta activity” Unlike original claims 3 and 4, which were directed to a method involving the actual physical crystal of HPTPbeta, claims 10-24 involve providing the atomic coordinates, rather than the actual physical crystal, for a crystalline form of HPTPbeta.

However, solely to expedite prosecution, claim 10 has been amended herein to delete the phrase “crystalline form.” As amended claim 10 clearly falls within elected Group II, Applicants respectfully request that the Examiner reinstate independent claim 10 and its dependent claims 11-24 for examination.

Compliance with 37 C.F.R. §§ 1.821–1.825

The Office Action maintains the contention that the instant Application does not comply with the sequence requirements of 37 C.F.R. §§ 1.821–1.825.

The Office Action dated November 22, 2006 stated that “the sequence identifier must be inserted each time after the phrase ‘HPTPbeta,’ wherever it appears.” Office Action dated November 22, 2006, page 2. In Applicants’ Amendment After Final Action under 37 C.F.R. § 1.116 dated May 21, 2007 (the “previous Reply”), Applicants set forth reasons why a sequence identification number after each occurrence of the term ‘HPTPbeta’ is not required.

While Applicants respectfully submit that the claims and specification do comply with the sequence requirements of §§ 1.821-1.821 for the reasons set forth in Applicants’ previous Reply, solely to expedite prosecution, Applicants submit herein amendments to the claims and a Substitute Specification that include the addition of sequence identification numbers after the relevant phrases involving HPTPbeta. In particular, the outstanding Office Action now states that “each time in the specification the phrase ‘HPTPbeta’ appear[s] to refer to a specific amino acid sequence or nucleic acid in the sequence listing, a sequence identification number should follow the phrase.” Office Action, page 2. Accordingly, it is Applicants’ understanding that the Office Action is no longer requiring Applicants to add a sequence identification number after each occurrence of the term “HPTPbeta” regardless of whether it “appear[s] to refer to a specific amino acid sequence or nucleic acid in the sequence listing.” Based on this understanding, amended claims 10-32 and the specification now list “SEQ ID NO: 7” after each occurrence of the phrase “HPTPbeta catalytic domain” that Applicants believe “appear[s] to refer to a specific amino acid sequence or nucleic acid in the sequence listing” in accordance with the Examiner’s statement in the current Office Action.

Rejection Under 35 U.S.C. § 112, ¶ 2

The Office Action states that claims 25-32 are rejected under 35 U.S.C. § 112, ¶ 2, as purportedly being indefinite.

The Office Action states that the phrase “imaging . . . a crystalline form of” in claims 25 and 26 is indefinite. Office Action, page 3. Without conceding the propriety of the rejection, and solely to expedite prosecution, claims 25 and 26 are amended to delete the phrase “crystalline form.” Therefore, as this aspect of the rejection of claims 25 and 26 is rendered moot, Applicants request that the Examiner withdraw at least this aspect of the rejection under § 112, ¶ 2.

The Office Action states that the phrase “HPTPbeta catalytic domain” in claims 25 and 26 “renders the claim indefinite” because “[t]he claim is not in compliance with the sequence rules.” *Id.* As stated above, claims 25 and 26 are amended herein to identify a sequence identification number in the manner suggested by the Examiner. Thus, without conceding the propriety of the § 112, ¶ 2 rejection, claims 25 and 26 identify SEQ ID NO: 7 after the occurrences of the phrase “HPTPbeta catalytic domain,” thereby rendering this aspect of the rejection of claims 25 and 26 under § 112, ¶ 2 moot. Consequently, Applicants request the Examiner to withdraw at least this aspect of the rejection under § 112, ¶ 2.

In view of the above, Applicants respectfully request that the Examiner withdraw the § 112, ¶ 2 rejection of independent claims 25 and 26 and claims 27-32 depending therefrom.

Rejection Under 35 U.S.C. § 103(a)

The Examiner rejects claims 25-32 under 35 U.S.C. § 103(a) as allegedly unpatentable over Cohen *et al.*, “Molecular Modeling Software and Methods for Medicinal Chemistry,” *J. Med. Chem.* 33(3):883-889 (1990) (the “Cohen reference”) in view of Fachinger *et al.*, “Functional Interaction of Vascular Endothelial-Protein-Tyrosine Phosphatase with the Angiopoietin Receptor Tie-2,” *Oncogene* 18:1189-1198 (1999) (the “Fachinger reference”). The Office Action states that “Cohen *et al.* [sic] the commercial availability of computers and various packages software used for imaging and identifying potential drugs using atomic coordinates of biological molecules.” Office Action, page 4. The Office Action further states that “Fachinger *et al.* teach a protein named VE-PTP and is functional interaction of a murine protein-tyrosine phosphatase with the angiopoietin Tie-2, see the abstract. Also, they teach that HPTPbeta is the human analog of VE-PTP.” *Id.* Applicants respectfully traverse this rejection.

For the first time, the Examiner cites the Trilateral Project WM4 Comparative Studies in New Technologies, Report on Comparative Study on Protein 3-Dimensional (3-D) Structure Related Claims (Nov. 4-8, 2002) (the “Trilateral Report”). However, it is unclear why the Examiner is relying on the Trilateral Report, which is not a legal authority. To the contrary, the Trilateral Report contains directives not contained in the case law or the M.P.E.P. For example, the Trilateral Report states that “the key factor in analyzing the obviousness of [] claims over the prior art is the determination that the computer algorithm used to identify compounds that can potentially bind protein [] is a known algorithm and unmodified.” *Id.* at 25; 72 (duplicate) (annex 3). Yet such a “key factor” in obviousness analyses is not set forth in the case law or in the M.P.E.P. The case law clearly states that the emphasis is on the claim *as a whole*: “Under sec. 103, the board cannot dissect a claim, excise [a new aspect] from it, and declare the remaining portion of the mutilated claim to be unpatentable.” *In re Gulak*, 703 F.2d 1381, 1385 (Fed. Cir. 1983) (cited by M.P.E.P. § 2106.01 at 2100-7 (8th rev., no. 5) “USPTO personnel must consider all claim limitations when determining patentability of an invention over the prior art.”).

The designation of the computer algorithm as the “key factor” in the Trilateral Report, and consequently the Office Action’s reliance on the Trilateral Report, is entirely misplaced. As set forth in Applicants’ previous Reply, “the critical question is whether there exists any new and unobvious functional relationship between the [descriptive] matter and [other features of the claim].” *Id.* at 1386 (quoted by M.P.E.P. § 2106.01 at 2100-50); *see also In re Lowry*, 32 F.3d 1579 (Fed. Cir. 1994) (“The PTO did not establish that the ADOs [attribute data objects], within the context of the entire claims, lack a new and nonobvious functional relationship with the memory. In sum, the ADOs perform a function. *Gulak* requires no more.” (citations omitted)) (cited by M.P.E.P. § 2106.01 at 2100-7).

To the extent the Office Action is considering a relationship at all in the claims of the instant Application, the Office Action focuses on the relationship between the computer algorithm and the atomic structure coordinates, which, according to the Trilateral Report, is presumptively obvious. As set forth in Applicants’ previous Reply, however, the proper focus is the relationship between the atomic structure coordinates and the drug candidate compound. The Office Action does not consider this relationship at all. Therefore, the obviousness analysis

set forth in the Office Action is not in accord with the established authoritative bodies, namely, Federal Circuit case law and the M.P.E.P. For at least this reason, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness.

Moreover, Applicants respectfully reiterate that the claimed methods of the invention are non-obvious over the Cohen reference in view of the Fachinger reference for at least the reason that Applicants claim a non-obvious functional and structural relationship between the three-dimensional coordinates of HPTPbeta and a drug candidate compound for the treatment of an angiogenesis mediated disorder. Applicants' claimed methods involve positioning a candidate compound at an area of an imaged HPTPbeta domain. This act of positioning a compound has a crucial functional and structural relationship with the coordinates. The coordinates define the three-dimensional structure of HPTPbeta in relation to space and in relation to itself. Thus, the coordinates are responsible for the special nature of the three-dimensional HPTPbeta structure. The positioning of the compound occurs relative to the three-dimensional HPTPbeta structure. One cannot position a compound in some orientation to an area of HPTPbeta without accessing this special nature of the three-dimensional structure. In this manner, the positioning of the compound is critically related to the unique three-dimensional coordinates of HPTPbeta, which the Examiner recognizes are novel. As in *Gulak*, the claimed feature "exploit[s]" the nature of another feature to which it is functionally related. *Gulak*, 703 F.2d at 1387. In Applicants' inventive methods, the use of X, Y and Z coordinates of HPTPbeta "exploits" the particular nature of a drug candidate compound, such as its binding properties, by rendering the candidate compound positioned at a unique area of the X, Y and Z-defined area of HPTPbeta. The X, Y and Z coordinates of HPTPbeta are also related to the drug candidate compound in that Applicants' inventive method involves identifying from a candidate compound those that bind or modulate the X, Y and Z-defined area of HPTPbeta as compounds useful for the treatment of an angiogenesis mediated disorder.

No aspect of the Cohen reference, the Fachinger reference or any other reference, considered alone or in combination, discloses, for example, a computer-implemented method involving determining a three-dimensional structure of all or a portion of an HPTPbeta catalytic domain from the recited X, Y and Z atomic structure coordinates of an HPTPbeta catalytic domain, and identifying drug candidate compounds from compounds that bind or modulate

HPTPbeta as compounds useful for the treatment of an angiogenesis mediated disorder. The cited documents cannot disclose or suggest this claimed subject matter because, as the Examiner recognizes, the atomic coordinates of HPTPbeta are novel. Even in light of knowledge imparted by the Cohen reference, the Fachinger reference and any other reference, because the coordinates of Applicants' invention were not known or suggested to one of skill in the art, the skilled person could not: (i) image a three-dimensional structure of an HPTPbeta catalytic domain; (ii) position candidate compounds at an area of the imaged three-dimensional structure; and (iii) identify candidate compounds that bind or modulate HPTPbeta as drug candidate compounds. Nothing in any of the references teaches or suggests to the skilled person what the unique three-dimensional coordinates of HPTPbeta are. Hence, the combination of the features recited in the claims that encompasses these coordinates is not rendered obvious by the cited documents.

For at least all of the foregoing reasons, Applicants respectfully submit that the rejection under § 103(a) cannot properly be maintained. Accordingly, Applicants respectfully request the Examiner to withdraw the rejection, and pass the claims to allowance.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment is respectfully requested.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

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Respectfully submitted,

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